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# Language and mathematical problems as precursors of psychotic-like experiences and juvenile mania symptoms

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**Background.** Psychotic-like experiences (PLEs) and juvenile mania in adolescence index risk for severe psychopathology in adulthood. The importance of childhood problems with communication, reading, speech and mathematics for the development of PLEs and juvenile mania is not well understood.

**Method.** Through the Child and Adolescent Twin Study in Sweden, we identified 5812 children. The parents were interviewed about their children's development at age 9 or 12 years. At age 15 or 18 years, children and parents completed questionnaires targeting current PLEs and juvenile mania symptoms. Logistic regressions were used to assess associations between problems with communication, reading, speech and mathematics and PLEs/juvenile mania symptoms. To evaluate the relative importance of genes and environment in these associations, we used bivariate twin analyses based on structural equation models.

**Results.** Children with parent-endorsed childhood problems with communication, reading and mathematics had an increased risk of developing auditory hallucinations and parental-reported juvenile mania symptoms in adolescence. The most consistent finding was that children with childhood problems with communication, reading and mathematics had an increased risk of developing auditory hallucinations [for example, the risk for self-reported auditory hallucinations at age 15 was increased by 96% for children with communication problems: OR (odds ratio) 1.96, 95% confidence interval (CI) 1.33–2.88]. The twin analyses showed that genetic effects accounted for the increased risk of PLEs and juvenile mania symptoms among children with communication problems.

**Conclusions.** Childhood problems with communication, reading and mathematics predict PLEs and juvenile mania symptoms in adolescence. Similar to the case for schizophrenia and bipolar disorder, PLEs and juvenile mania may share genetic aetiological factors.

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**Key words:** Juvenile mania symptoms, language problems, mathematical problems, psychotic-like experiences.

## Introduction

Children who will later develop schizophrenia exhibit neurodevelopmental problems, such as problems with the development of language and mathematics (Kolvin *et al.* 1971; Crow *et al.* 1995). Recently, research has started to explore associations between neurodevelopmental problems and psychotic symptoms in non-clinical populations, commonly referred to as

psychotic-like experiences (PLEs). PLEs index increased risk for clinical psychosis (Poulton *et al.* 2000) and almost the same spectrum of risk factors applies to PLEs and clinical psychosis (van Os *et al.* 2009; Polanczyk *et al.* 2010). Notably, in a validation study, only auditory hallucinations had good positive and negative predictive values for clinically verifiable PLEs (Kelleher *et al.* 2011). Thus, the relatively large group of children with PLEs, chiefly auditory hallucinations, may represent a valuable population for aetiological psychosis research. The possible importance of childhood problems with communication, reading and mathematics in the development of adolescent PLEs remains unexplored, but an association between

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speech problems and PLEs was indicated recently (Bevan Jones *et al.* 2012).

Juvenile mania is a childhood-onset mood disorder that is associated with a range of adverse effects (Pavuluri *et al.* 2005). In contrast to adult-onset bipolar disorder, juvenile mania is marked by childhood developmental problems (Murray *et al.* 2004). However, the evidence for language problems is inconclusive; van Os *et al.* (1997) and Sigurdson *et al.* (1999) have reported speech problems in children who will later develop juvenile mania whereas other studies indicate normal pre-morbid functioning on tasks related to language (Kutcher *et al.* 1998).

The aim of the current study was to determine whether childhood problems with communication, reading, speech and mathematics are associated with PLEs and juvenile mania in two samples of Swedish twins, using multiple informants. In addition, we wanted to disentangle genetic from environmental factors behind the observed associations.

## Method

### Participants

The Child and Adolescent Twin Study in Sweden (CATSS) is an ongoing longitudinal study targeting all twins born in Sweden since 1992 (current  $n = 11\,000$  twin pairs). In connection with the children's 9th or 12th birthdays, the parents are interviewed about their children's development (CATSS-9/12). The present study is based on the 5812 children who also have data on a follow-up at age 15 or 18 years; 1966 children were aged 9 years at the time of the CATSS-9/12 interview and 3846 were aged 12 years. At age 15 or 18 years, twins and their parents completed separate questionnaires targeting current PLEs and juvenile mania symptoms (Anckarsäter *et al.* 2010). The total sample consisted of two groups: in one group ( $n = 3809$ ) the questionnaires were completed at age 15 (the CATSS-15 sample) and in the other group ( $n = 2003$ ) the questionnaires were completed at age 18 (the CATSS-18 sample). Only 134 individuals overlapped between the two samples. A subgroup of the total sample ( $n = 349$ ) who screened positive for neuropsychiatric disorders in the CATSS-9/12 interview responded to the CATSS-15 questionnaire regarding clinical examination. Three children were excluded from the analyses because of chromosomal syndromes resulting in mental retardation. The response rate was 80% in the CATSS-9/12 interview and 49%, for both children and parents, in the CATSS-15 sample. In the CATSS-18 sample, the response rate was 47% for the children and 45% for the parents. Ethical approval was obtained from the

Regional Ethical Review Board in Stockholm and informed consent was obtained from all participants.

### Measures of problems with communication, reading, speech and mathematics

The Autism-Tics, AD/HD and other Comorbidities inventory (A-TAC; Hansson *et al.* 2005; Larson *et al.* 2010) was used to screen for problems with communication, reading, speech and mathematics. The items in the A-TAC are organized in modules (e.g. concentration and attention, social interaction, language) and all questions refer to a lifetime perspective in comparison to peers. For each question, the response alternatives are: 'yes' (scored 1), 'yes, to some extent' (scored 0.5), 'no' (scored 0), 'do not know' and 'do not wish to answer' (both scored as missing).

Communication problems were targeted with four questions concerning conversations, word repetitions, high voice pitch or quiet speech and monotonous speech. A sum scale of communication problems was created, with a cut-off at 0.5. The prevalence of communication problems defined this way was 13.1% (Table 1). Problems with speech (delayed speech development), reading (delayed reading development) and mathematics were targeted with one item each, with a cut-off of 1 for reading problems and 0.5 for problems with speech and mathematics. Based on this, 7.3, 9.4 and 12.7% of children were classified with reading, speech and mathematical problems respectively (Table 1).

### Measures of PLEs

In the CATSS-15 sample, children and parents were asked eight questions targeting hallucinations (auditory, visual) and delusions (persecution, thought interference, reference, control, special powers, thought broadcasting). The items were derived from previous studies on community samples (Poulton *et al.* 2000; Laurens *et al.* 2007). In the CATSS-18 sample, only auditory hallucinations were measured. The children had four possible responses in the CATSS-15 sample: 'yes' (scored 1), 'no' (scored 0), 'do not know' and 'do not wish to answer' (both scored as missing). They had five responses in the CATSS-18 sample: 'yes' (scored 2), 'yes, to some extent' (scored 1), 'no' (scored 0), 'do not know' and 'do not wish to answer'. For parents in both samples the responses were 'yes', 'yes, to some extent', 'no', 'do not know' and 'do not wish to answer', which were scored as the children's answers. In a validation study, only auditory hallucinations had good positive and negative predictive values for clinically verifiable PLEs (Kelleher *et al.* 2011). Therefore, in this study, auditory hallucinations

**Table 1.** Descriptive statistics

	Communication problems		Reading problems		Speech problems		Mathematical problems	
	Yes	No	Yes	No	Yes	No	Yes	No
Number (%) with the problem	761 (13.1)	5051 (86.9)	421 (7.3)	5363 (82.7)	548 (9.4)	5264 (90.6)	738 (12.7)	5074 (81.3)
Sex								
Male	378 (49.7)	2392 (47.4)	263 (62.5)	2490 (46.4)	357 (65.2)	2413 (45.8)	299 (40.5)	2471 (48.7)
Female	383 (50.3)	2659 (52.6)	158 (37.5)	2873 (53.6)	191 (34.8)	2851 (54.2)	439 (59.5)	2603 (51.3)
SES								
Low	117 (15.5)	561 (11.2)	64 (15.4)	614 (11.5)	65 (12.0)	613 (11.7)	136 (18.6)	542 (10.8)
Intermediate	464 (61.5)	2973 (59.4)	264 (63.5)	3159 (59.3)	340 (62.5)	3097 (59.4)	464 (63.4)	2973 (59.1)
High	174 (23.0)	1472 (29.4)	88 (21.1)	1555 (29.2)	139 (25.5)	1507 (28.9)	132 (18.0)	1514 (30.1)
Residential area								
Large city	196 (26.0)	1189 (23.7)	85 (20.4)	1298 (24.3)	122 (22.4)	1263 (24.2)	180 (24.6)	1205 (24.0)
Medium city	320 (42.3)	2228 (44.5)	192 (46.2)	2344 (44.0)	252 (46.2)	2296 (44.0)	316 (43.1)	2232 (44.3)
Rural area	239 (31.7)	1593 (31.8)	139 (33.4)	1689 (31.7)	171 (31.4)	1661 (31.8)	237 (32.3)	1595 (31.7)

SES, Socio-economic status.

Values given as *n* (%).

were analysed separately. We also created a sum scale of 'other PLEs', that is all PLEs except auditory hallucinations.

### Measures of juvenile mania symptoms

In the CATSS-15 sample, the Child Mania Rating Scale – Parent Version (CMRS-P; Henry *et al.* 2008) was used as the screening instrument. Children and parents were asked questions targeting elated mood, irritability, over-energy, grandiosity, less need for sleep, racing thoughts, fast talk, rage attacks and sexually inappropriate behaviour. In the CATSS-18 sample, the Mood Disorder Questionnaire (MDQ; Hirschfeld *et al.* 2000) and part of the CMRS-P were used. The items from the MDQ that corresponded to the CMRS-P items in the CATSS-15 study were used in the CATSS-18, but self-reports of rage attacks and parent reports of grandiosity, fast talk, racing thoughts and rage attacks were not asked for. Sum scales were calculated by adding the scores from the juvenile mania items that were included in the respective studies for self-reports and parent reports separately.

### Covariates

The following variables may be associated with problems with communication, reading, speech or mathematics in addition to PLEs or juvenile mania symptoms and were therefore included as covariates: sex, socio-economic status (SES), main city residence, autism spectrum disorders, attention deficit hyper-

activity disorder (ADHD), conduct disorder, obsessive-compulsive disorder, learning disorder and developmental coordination disorder. The parent's educational level was used as a proxy for SES, and for these questions there were eight responses classified into low (elementary and grade school), intermediate (junior secondary school, vocational school, military school, 2–4 years high school and residential high school) and high (university  $\geq 2$  years) SES. The highest educational level within a family was used. The A-TAC provides cut-off levels based on DSM-IV criteria for the neuropsychiatric disorders considered (Larson *et al.* 2010), and variables that coded for neuropsychiatric caseness based on these cut-offs were used in the regression models. The variables targeting problems with communication, reading, speech and mathematics were included in already validated measures of learning problems and autism spectrum disorder. Including these measures of neuropsychiatric disorders as covariates in the statistical models therefore tests the unique effects of communication, reading, speech and mathematical problems after controlling for fulfilment of the criteria for the disorders.

### Statistical analysis

The measures of PLEs and juvenile mania symptoms were binary or ordered categories, so we assessed associations between problems with communication, reading, speech and mathematics and PLEs/juvenile mania symptoms using binary and ordered logistic regressions. As several correlated twin pairs could

**Table 2.** Frequencies of auditory hallucinations, other PLEs and juvenile mania symptoms

	Range	0	1	2	3	4	≥5
CATSS-15							
Auditory hallucinations							
Self-reports	0–3	3528 (95.6)	131 (3.6)	15 (0.4)	16 (0.4)		
Parent reports	0–3	3391 (99.5)	15 (0.4)	1 (0.03)	1 (0.03)		
Other PLEs							
Self-reports	0–7	1175 (31.6)	945 (25.4)	748 (20.1)	461 (12.4)	236 (6.4)	152 (4.1)
Parent reports	0–14	2712 (79.4)	421 (12.3)	162 (4.8)	54 (1.6)	41 (1.2)	26 (0.7)
Juvenile mania symptoms							
Self-reports	0–27	397 (10.7)	315 (8.5)	420 (11.3)	482 (13.0)	429 (11.5)	1673 (58.0)
Parent reports	0–27	114 (3.3)	1672 (49.0)	364 (10.7)	403 (11.8)	306 (9.0)	557 (16.2)
CATSS-18							
Auditory hallucinations							
Self-reports	0–3	1583 (95.8)	57 (3.4)	5 (0.3)	8 (0.5)		
Parent reports	0–3	1512 (99.2)	11 (0.7)	2 (0.1)			
Juvenile mania symptoms							
Self-reports	0–8	308 (18.5)	278 (16.7)	283 (17.0)	266 (16.0)	258 (15.5)	269 (16.3)
Parent reports	0–8	1098 (71.6)	236 (15.4)	126 (8.2)	41 (2.7)	24 (1.6)	8 (0.5)

PLE, Psychotic-like experiences; CATSS, Child and Adolescent Twin Study in Sweden (CATSS-15 and -18 questionnaires completed at age 15 and 18 years respectively).

Values given as *n* (%).

be included in an analysis, a robust sandwich estimator was used to adjust for the correlated data when calculating the confidence intervals (CIs). For the twin analyses, we used the maximum likelihood method to calculate polychoric correlations between problems with communication, reading, speech, mathematics and PLEs/juvenile mania symptoms. All statistical analyses were performed in SAS version 9.3 (SAS Institute Inc., 2012) and Stata version 12 (Stata-Corp, 2011).

### Genetic analyses

Twin methodology relies on the genetic relatedness of monozygotic (MZ) *versus* dizygotic (DZ) twins. If a trait is influenced by genes, there will be a higher similarity within MZ twin pairs than within DZ twin pairs. Twin analyses can be used to estimate the relative importance of genetic and environmental effects on one or more traits (Rijsdijk & Sham, 2002). The variation in a phenotype can then be decomposed into three factors: additive genetics, shared environment (factors that make twins alike) and non-shared environment (factors that make twins different). In this study, bivariate twin analyses were used to decompose the phenotypic covariation between childhood communication problems and self-reported auditory hallucinations, parent-reported other PLEs and parent-reported juvenile mania symptoms at age 15

into these three factors, using the so-called Cholesky decomposition. The phenotypic outcomes (auditory hallucinations, other PLEs, juvenile mania symptoms) were regressed on the genetic, shared environment and unique environment factors of the predictor variable (communication problems). Because the variables were highly skewed and the responses were ordered categories, the model was estimated using weighted least squares with a mean and variance-adjusted  $\chi^2$  statistic using Mplus version 6.11 (Muthén & Muthén, 1998–2010).

## Results

### Descriptive statistics

Sample characteristics are shown in Table 1. More male than female children had speech problems and reading problems whereas more female than male children had mathematical problems. Compared with controls, low SES was more common in families with communication, reading, speech and mathematical problems whereas there did not seem to be any difference in urbanicity. The frequencies of PLEs and juvenile mania symptoms are shown in Table 2. Typical of such psychiatric symptoms data, each distribution was highly skewed, with the exception of self-reports of juvenile mania symptoms.

**Table 3.** Associations between problem with communication, reading, speech and mathematics in childhood and PLEs at ages 15 and 18 years

		CATSS-15			CATSS-18		
	Rater	Crude OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)	Corr.	Crude OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)	Corr.
Auditory hallucinations							
Communication problems	Child	<b>1.96 (1.42–2.69)</b>	<b>1.96 (1.33–2.88)</b>	0.19	<b>2.01 (1.20–3.34)</b>	<b>1.87 (1.13–3.07)</b>	0.20
	Parent	<b>3.59 (2.21–5.85)</b>	2.33 (0.89–6.10)	0.38	2.08 (0.71–6.08)	0.87 (0.19–4.01)	0.14
Reading problems	Child	1.14 (0.66–1.95)	1.15 (0.66–2.01)	0.03	<b>2.43 (1.13–5.21)</b>	2.00 (0.85–4.71)	0.19
	Parent	<b>5.20 (1.33–20.26)</b>	3.75 (0.93–15.08)	0.28	<b>7.32 (2.19–24.51)</b>	<b>5.54 (1.04–29.51)</b>	0.34
Speech problems	Child	0.96 (0.48–1.94)	0.98 (0.48–2.01)	–0.02	1.16 (0.43–3.08)	1.35 (0.53–3.44)	0.01
	Parent	3.17 (0.73–13.72)	1.99 (0.33–12.16)	0.17	3.38 (0.76–15.03)	1.66 (0.20–13.88)	0.20
Mathematical problems	Child	<b>1.84 (1.04–3.23)</b>	1.68 (0.91–3.10)	0.11	<b>2.76 (1.08–7.06)</b>	1.62 (0.61–4.29)	0.18
	Parent	<b>5.93 (1.10–31.98)</b>	1.54 (0.22–10.63)	0.24	<b>7.19 (1.82–28.33)</b>	5.27 (0.78–35.62)	0.29
Other PLEs							
Communication problems	Child	1.15 (0.94–1.40)	<b>1.25 (1.00–1.55)</b>	0.07			
	Parent	<b>1.56 (1.21–2.01)</b>	<b>1.69 (1.27–2.25)</b>	0.15			
Reading problems	Child	<b>0.69 (0.56–0.86)</b>	<b>0.72 (0.57–0.92)</b>	–0.09			
	Parent	0.86 (0.62–1.20)	0.97 (0.68–1.38)	–0.03			
Speech problems	Child	<b>0.68 (0.51–0.90)</b>	0.83 (0.62–1.11)	–0.08			
	Parent	1.16 (0.75–1.79)	1.43 (0.92–2.20)	0.04			
Mathematical problems	Child	0.94 (0.74–1.19)	0.82 (0.63–1.07)	–0.01			
	Parent	1.31 (0.92–1.87)	1.27 (0.86–1.88)	0.06			

PLEs, Psychotic-like experiences; CATSS, Child and Adolescent Twin Study in Sweden (CATSS-15 and -18 questionnaires completed at age 15 and 18 years respectively); OR, odds ratio; CI, confidence interval; Corr., polychoric correlation.

<sup>a</sup> Adjusted for sex, socio-economic status (SES), urbanicity and neurodevelopmental problems.

Statistically significant ORs are shown in bold.

### Problems with communication, reading, speech and mathematics as predictors of PLEs and juvenile mania symptoms

Compared to children without parent-endorsed childhood problems with communication, reading and mathematics, children with these problems had an increased risk of developing auditory hallucinations in adolescence (Table 3). These increased risks were found regardless of whether self-reports or parent reports were used. For example, there was an increased risk for self-reported auditory hallucinations in children with communication problems (OR 1.96) that remained unchanged after controlling for sex, educational level, urbanicity and neurodevelopmental problems (OR 1.96). For one unit increase in childhood communication problems (e.g. going from 0 to 0.5), the risk of reporting auditory hallucinations at age 15 increased by 96%. Problems with communication, reading, speech or mathematics did not seem to be predictive of PLEs other than auditory hallucinations (Table 3).

Problems with communication, reading and mathematics were important for the development of parent-reported juvenile mania symptoms (Table 4; e.g. for communication problems, OR was 1.28), but there

was less evidence for associations between these problems and self-reported juvenile mania symptoms.

### Genetic analyses

Where significant associations were found, we continued with genetic analyses to determine whether the effects were genetically or environmentally mediated. All associations with polychoric correlations > 0.15 were examined (Tables 3 and 4). As the scores of parent-reported juvenile mania symptoms ranged from 0 to 18, where a score of 1 was much more frequent than a score of 0 (Table 2), we created a new variable with four categories. This variable had a polychoric correlation with communication problems of 0.21. Because the shared environment factor did not contribute to variation in communication problems, it was excluded from the models. It was possible to identify solutions for the associations between communication problems and self-reported auditory hallucinations, parent-reported other PLEs and parent-reported juvenile mania symptoms at age 15, whereas power or distributional problems made it impossible to identify solutions for the remainder of the associations. The bivariate Cholesky decomposition demonstrated that additive genetic effects



**Table 4.** Associations between problems with communication, reading, speech and mathematics in childhood and juvenile mania symptoms at age 15 and 18 years

	Rater	CATSS-15			CATSS-18		
		Crude OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)	Corr.	Crude OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)	Corr.
Communication problems	Child	1.04 (0.88–1.24)	1.16 (0.96–1.39)	0.02	1.26 (0.83–1.93)	1.21 (0.81–1.81)	0.06
	Parent	<b>2.04 (1.55–2.69)</b>	<b>1.62 (1.24–2.12)</b>	0.18	<b>1.70 (1.17–2.46)</b>	<b>1.61 (1.03–2.52)</b>	0.15
Reading problems	Child	<b>0.57 (0.46–0.71)</b>	<b>0.60 (0.47–0.76)</b>	–0.14	1.07 (0.78–1.48)	1.08 (0.78–1.51)	0.01
	Parent	1.32 (0.99–1.74)	1.17 (0.88–1.55)	0.06	<b>1.52 (1.03–2.24)</b>	1.27 (0.80–2.02)	0.10
Speech problems	Child	0.76 (0.58–1.00)	0.87 (0.65–1.16)	–0.06	0.94 (0.69–1.30)	0.97 (0.71–1.32)	–0.01
	Parent	1.14 (0.81–1.62)	1.05 (0.74–1.49)	0.04	1.21 (0.78–1.90)	1.17 (0.71–1.94)	0.03
Mathematical problems	Child	0.79 (0.62–1.02)	0.77 (0.57–1.03)	–0.14	1.23 (0.85–1.78)	1.20 (0.81–1.78)	0.03
	Parent	<b>1.79 (1.29–2.49)</b>	<b>1.48 (1.07–2.04)</b>	0.11	<b>2.32 (1.46–3.71)</b>	<b>2.08 (1.18–3.67)</b>	0.17

CATSS, Child and Adolescent Twin Study in Sweden (CATSS-15 and -18 questionnaires completed at age 15 and 18 years respectively); OR, odds ratio; CI, confidence interval; Corr., polychoric correlation.

<sup>a</sup> Adjusted for sex, socio-economic status (SES), urbanicity and neurodevelopmental problems.

Statistically significant ORs are shown in bold.

**Table 5.** Genetic and environmental effects on the association between communication problems and auditory hallucinations, other PLEs and juvenile mania symptoms

Predictor	Outcome	Standardized $\beta$	
		Additive genetic effects	Unique environmental effects
Communication problems	Auditory hallucinations	0.16*	–0.02, n.s.
Communication problems	Other PLEs	0.09**	–0.03, n.s.
Communication problems	Juvenile mania symptoms	0.21**	–0.03, n.s.

PLEs, Psychotic-like experiences; n.s., not significant.

\*  $p < 0.05$ , \*\*  $p < 0.001$ .

accounted for essentially the entire association between communication problems and both auditory hallucinations, other PLEs and juvenile mania symptoms, and that unique environmental effects were not important for any of these associations (Table 5). For further details of the twin analyses, see the online Supplementary material.

## Discussion

We found that children with parent-endorsed childhood problems with communication, reading and mathematics had an increased risk of developing both PLEs and juvenile mania symptoms in adolescence. However, it seems that problems with communication, reading and mathematics were important primarily with respect to auditory hallucinations, but not other PLEs, and that they predicted parent-

reported, but not self-reported, juvenile mania symptoms. Where significant associations were found and it was possible to perform twin analyses, the results indicate that the associations were entirely due to common genetic susceptibilities.

Pre-morbid communication problems have previously been found in early-onset cases of schizophrenia (Hollis, 1995) and the findings in the current study suggest that these problems may also be evident in children who will later develop PLEs/juvenile mania symptoms. The associations between reading problems and PLEs/juvenile mania symptoms were inconsistent. Of note, reading problems have recently been found to be specifically associated with core features of schizophrenia (i.e. auditory hallucinations) but not with schizotypal traits (i.e. other PLEs; Rössler et al. 2011). Our results are partially in keeping with these findings, as reading problems were associated with some measures

of auditory hallucinations but not other PLEs. The absence of an association between speech problems and PLEs is largely consistent with previous PLE research (Cannon *et al.* 2002), although Bevan Jones *et al.* (2012) recently reported such an association. However, in the latter study PLEs were assessed at age 12, when PLEs may be part of a more typical development than at age 15 and 18, when they are likely to be more pathological (Kelleher *et al.* 2012; Murray & Jones, 2012). In contrast to previous studies (van Os *et al.* 1997; Sigurdson *et al.* 1999), we did not find strong evidence for associations between speech problems and juvenile mania symptoms. However, previous studies used teacher's reports (van Os *et al.* 1997) or register information (Sigurdson *et al.* 1999) to define juvenile mania, which may have different clinical properties than self-reports and parent reports. Mathematical problems have previously been found in children who will later develop schizophrenia (Crow *et al.* 1995), and the associations observed in the current study indicate that mathematical problems may already be present in childhood in children who will later develop PLEs and juvenile mania symptoms. Taken together, it seems that problems with communication, reading and mathematics are precursors of PLEs and juvenile mania symptoms, consistent with the picture in schizophrenia. Thus, as noted previously (Polanczyk *et al.* 2010; Kelleher *et al.* 2011), children with PLEs, a large group compared to clinical cases, are likely to be a valuable population for aetiological psychosis research.

The twin analyses showed that there was a common genetic susceptibility for communication problems and self-reported auditory hallucinations, parent-reported other PLEs and parent-reported juvenile mania symptoms at age 15, as genetic factors accounted for essentially the entire phenotypic correlations. These findings suggest that PLEs and juvenile mania symptoms share some common genetic factors with communication problems, which may indicate that, as in schizophrenia and bipolar disorder (Lichtenstein *et al.* 2009), PLEs and juvenile mania symptoms share common genetic factors.

Previous research suggests that auditory hallucinations are the most valid and clinically significant measure of PLEs (Kelleher *et al.* 2011). Our data are consistent with this notion, and future research should ensure that this symptom is included when screening for PLEs. In large population-based studies it is often necessary to use as few items as possible, and in that context we suggest that auditory hallucinations are the most useful symptoms to enquire about.

Through the use of multiple informants, we found that parent reports of PLEs were substantially less common than self-reports in both samples, which

raises questions about the pathological significance of parent- *versus* self-reported PLEs. It is possible that adults may more easily grasp the psychotic values of PLEs than some adolescents, but parents may also not be aware of their children's PLEs as they may tend to keep them to themselves (Laurens *et al.* 2007). However, we did not find any clear evidence of a difference in how the problems with communication, reading, speech and mathematics predicted self-reports and parent reports of PLEs. This was not the case for juvenile mania symptoms, where only parent reports were associated with problems with communication, reading and mathematics. In a previous study on Swedish twins (Chang *et al.* 2013), self-reports of ADHD, which is clinically similar to juvenile mania (Pavuluri *et al.* 2005), were found to be more prone to contributions of measurement error than parent reports. Thus, we suggest that parent reports of juvenile mania symptoms are likely to be a more useful measure than self-reports.

### *Possible explanations*

There are several possible explanations for the associations observed between problems with communication, reading and mathematics and PLEs/juvenile mania symptoms. It is conceivable that the same genes underlie susceptibility for these childhood problems and PLEs/juvenile mania symptoms, and it has been proposed that the genetic endowment that makes human language possible is evolutionarily related to psychosis (Crow *et al.* 1995). Another possible explanation, which does not contradict the notion of shared genetic susceptibility, is that language problems and psychosis represent one disorder with diverse manifestations at different stages of development, in line with the concept of heterotypic continuity (Rutter *et al.* 2006). Through the use of twin analyses, we were able to take one step further in answering these questions, and the results support the notion of shared genetic susceptibility because essentially the entire phenotypic correlations between communication problems and self-reported auditory hallucinations, parent-reported other PLEs and parent-reported juvenile mania symptoms at age 15 were explained by genetic factors. To our knowledge, this is the first demonstration of the importance of genes in associations between communication problems in childhood and psychotic/affective symptoms in adolescence.

### *Strengths and limitations*

This study has several strengths. To date, it is the only evaluation of the developmental characteristics of both



PLEs and juvenile mania symptoms in two largely independent samples with participants at two different ages. It is also the first study to use multiple informants of PLEs and juvenile mania symptoms. As far as we know, this study is also the first prospective, longitudinal study to assess associations between childhood problems with reading and mathematics and PLEs, in addition to revealing the relative importance of genes and environment in the observed associations. However, the results in this study should be considered in the context of its limitations. We did not have the opportunity to study precursors of PLEs other than auditory hallucinations in the CATSS-18 sample. Furthermore, all measures relied on self-reports and parent reports, which are less reliable than direct clinical testing, although clinical examinations are not feasible in large epidemiological studies. The response rates in the CATSS-15 and -18 studies were fairly low, and it is possible that children with neurodevelopmental problems and psychiatric symptoms, and also their parents, were more prone to decline participation. This is unlikely, however, as attrition analyses revealed little difference between responders and non-responders in the CATSS-9/12 study (Anckarsäter et al. 2010). Moreover, the A-TAC is not formally validated for detection of problems with communication, reading, speech or mathematics, which may have led to some misclassifications of children with such problems. Nevertheless, it is validated to detect other neurodevelopmental problems, where facets of problems with communication, reading, speech and mathematics are included (Hansson et al. 2005; Larson et al. 2010). Furthermore, despite the fairly large sample size, children with parent-reported auditory hallucinations were few, which prohibited genetic analyses on these measures.

The fact that we did not find any significant effects of unique environmental factors on the observed associations was unexpected; it is well known, for example, that childhood trauma is associated with PLEs (Janssen et al. 2004). One explanation could be that the lack of unique environmental effects for the associations is due to limited power (for example, the confidence interval for the unique environmental parameter was  $-0.11$  to  $0.07$  for the association between communication problems and auditory hallucinations). Another explanation could be that the association between childhood trauma and PLEs is due to genetic effects; genetic effects are important for ostensible environmental influences (Plomin et al. 2001) and associations between childhood trauma and other outcomes, such as adult violent offending (Forsman & Långström, 2012), have been shown to be confounded by genetic effects. Nevertheless, larger studies and/or replications are warranted.

## Conclusions

Taken together, our findings suggest that children who display problems with communication, reading or mathematics have an increased risk of developing PLEs and juvenile mania symptoms in adolescence, which further corroborates the existence of neurodevelopmental deviations in PLEs and juvenile mania symptoms (van Os et al. 1997; Polanczyk et al. 2010). Genetic factors were found to be of importance in these associations. The similar pattern of risk factors for PLEs and juvenile mania symptoms observed in this study also implies shared aetiological factors, which may have implications for molecular genetic research. Thus, the emerging research field of PLEs should consider including symptoms of juvenile mania symptoms and extend the concept of PLEs to also include affective dimensions. Clinical practice may be enhanced through consideration of childhood and co-existing problems with communication, reading and mathematics in children with PLEs and juvenile mania symptoms, as they may have a negative impact on patient function. In addition, cross-professional monitoring of the development of children with problems with communication, reading or mathematics may facilitate early identification of PLEs and juvenile mania symptoms, which in turn may reduce the negative consequences.

## Supplementary material

For supplementary material accompanying this paper, please visit <http://dx.doi.org/10.1017/S0033291713002018>.

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## Declaration of Interest

None.

## References

- Anckarsäter H, Lundström S, Kollberg L, Kerekes N, Palm C, Carlström E, Långström N, Magnusson P, Halldner L, Bölte S, Gillberg C, Gumpert C, Råstam M, Lichtenstein P (2010). The Child and Adolescent Twin Study in Sweden (CATSS). *Twin Research and Human Genetics* **14**, 495–508.
- Bevan Jones R, Thapar A, Lewis G, Zammit S (2012). The association between early autistic traits and psychotic experiences in adolescence. *Schizophrenia Research* **135**, 164–169.

- Cannon M, Caspi A, Moffitt TE, Harrington H, Taylor A, Murray RM, Poulton R (2002). Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder. *Archives of General Psychiatry* 59, 449–456.
- Chang Z, Lichtenstein P, Asherson PJ, Larsson H (2013). Developmental twin study of attention problems: high heritabilities throughout development. *Journal of the American Medical Association Psychiatry* 70, 311–318.
- Crow TJ, Done DJ, Sacker A (1995). Childhood precursors of psychosis as clues to its evolutionary origins. *European Archives of Psychiatry and Clinical Neuroscience* 245, 61–69.
- Forsman M, Långström N (2012). Child maltreatment and adult violent offending: population-based twin study addressing the ‘cycle of violence’ hypothesis. *Psychological Medicine* 42, 1977–1983.
- Hansson SL, Svanström Röjvall A, Råstam M, Gillberg C, Gillberg IC, Anckarsäter H (2005). Psychiatric telephone interview with parents for screening of childhood autism - tics, attention-deficit hyperactivity disorder and other comorbidities (A-TAC): preliminary reliability and validity. *British Journal of Psychiatry* 87, 262–267.
- Henry DB, Pavuluri MN, Youngstrom E, Birmaher B (2008). Accuracy of brief and full forms of the Child Mania Rating Scale. *Journal of Clinical Psychology* 64, 368–381.
- Hirschfeld R, Williams JBW, Spitzer RL, Calabrese JR, Flynn L, Keck PE, Lewis L, McElroy SL, Post RM, Rapoport DJ, Russell JM, Sachs GS, Zajecka J (2000). Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. *American Journal of Psychiatry* 157, 1873–1875.
- Hollis C (1995). Child and adolescent (juvenile onset) schizophrenia. A case-control study of premorbid developmental impairments. *British Journal of Psychiatry* 166, 489–495.
- Janssen I, Krabbendam L, Bak M, Hanssen M, Volleberg W, de Graaf R, van Os J (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica* 109, 38–45.
- Kelleher I, Harley M, Murtagh A, Cannon M (2011). Are screening instruments valid for psychotic-like experiences? A validation study of screening questions for psychotic-like experiences using in-depth clinical interview. *Schizophrenia Bulletin* 37, 362–369.
- Kelleher I, Keeley H, Corcoran P, Lynch F, Fitzpatrick C, Devlin N, Molloy C, Clarke MC, Harley M, Arseneault L, Wasserman C, Carli V, Hoven C, Wasserman D, Cannon C (2012). Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *British Journal of Psychiatry* 201, 26–32.
- Kolvin I, Ounsted C, Humphrey M, McNay A (1971). The phenomenology of childhood psychoses. *British Journal of Psychiatry* 118, 385–395.
- Kutcher S, Robertson HA, Bird D (1998). Premorbid functioning in adolescent onset bipolar I disorder: a preliminary report from an ongoing study. *Journal of Affective Disorders* 51, 137–144.
- Larson T, Anckarsäter H, Gillberg C, Ståhlberg O, Carlström E, Kadesjö B, Råstam M, Lichtenstein P, Gillberg C (2010). The Autism - Tics, AD/HD and other Comorbidities inventory (A-TAC): further validation of a telephone interview for epidemiological research. *BMC Psychiatry* 10, 1.
- Laurens KR, Hodgins S, Maughan B, Murray RM, Rutter ML, Taylor EA (2007). Community screening for psychotic-like experiences and other putative antecedents of schizophrenia in children aged 9–12 years. *Schizophrenia Research* 90, 130–146.
- Lichtenstein P, Yip BH, Björk C, Pawitan Y, Cannon TD, Sullivan PF, Hultman CM (2009). Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. *Lancet* 373, 234–239.
- Murray GK, Jones PB (2012). Psychotic symptoms in young people without psychotic illness: mechanisms and meaning. *British Journal of Psychiatry* 201, 4–6.
- Murray RM, Sham P, van Os J, Zanelli J, Cannon M, McDonald C (2004). A developmental model for similarities and dissimilarities between schizophrenia and bipolar disorder. *Schizophrenia Research* 71, 405–416.
- Muthén LK, Muthén BO (1998–2010). *Mplus User’s Guide*, 6th edn. Muthén & Muthén: Los Angeles, CA.
- Pavuluri M, Birmaher B, Naylor MW (2005). Pediatric bipolar disorder: a review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry* 44, 846–871.
- Plomin R, Asbury K, Dip PG, Dunn J (2001). Why are children in the same family so different? Nonshared environment a decade later. *Canadian Journal of Psychiatry* 46, 225–233.
- Polanczyk G, Moffitt TE, Arseneault L, Cannon M, Ambler M, Keefe RSE, Houts R, Odgers CL, Caspi A (2010). Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. *Archives of General Psychiatry* 67, 328–338.
- Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H (2000). Children’s self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. *Archives of General Psychiatry* 57, 1053–1058.
- Rijsdijk FV, Sham PC (2002). Analytic approaches to twin data using structural equation models. *Briefings in Bioinformatics* 3, 119–133.
- Rössler W, Vetter S, Muller M, Gallo WT, Haker H, Kawohl W, Lupi G, Ajdacic-Gross V (2011). Risk factors at the low end of the psychosis continuum: much the same as at the upper end? *Psychiatry Research* 189, 77–81.
- Rutter M, Kim-Cohen J, Maughan B (2006). Continuities and discontinuities in psychopathology between childhood and adult life. *Journal of Child Psychology and Psychiatry* 47, 276–295.
- Sigurdson E, Fombonne E, Sayal K, Checkley S (1999). Neurodevelopmental antecedents of early-onset

- bipolar affective disorder. *British Journal of Psychiatry* **174**, 121–127.
- SAS Institute Inc.** (2012). *Base SAS® 9.3 Procedures Guide*. SAS Institute Inc.: Cary, NC.
- StataCorp** (2011). *Stata Statistical Software: Release 12*. StataCorp LP: College Station, TX.
- van Os J, Jones P, Lewis G, Wadsworth M, Murray M** (1997). Developmental precursors of affective illness in a general population birth cohort. *Archives of General Psychiatry* **54**, 625–631.
- van Os J, Linscott RJ, Myin-Germeys I, Delespaul P, Krabbendam L** (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. *Psychological Medicine* **39**, 179–195.